

REMARKS

I. Status of the claims

Claims 1-23, 28, 29, and 39-44 are pending in this application. Claims 3, 9, and 41-44 have been withdrawn by the Office for being directed to non-elected subject matter. No claim has been amended in this Response.

II. Rejections under 35 U.S.C. § 103

a. Claims 1, 2, 4, 7, 8, 11-13, 16, 17, 22, 23, 28, and 29

The Office rejected claims 1, 2, 4, 7, 8, 11-13, 16, 17, 22, 23, 28, and 29 under 35 U.S.C. 103(a) as allegedly being unpatentable over U.S. Patent No. 4,946,870 ("*Partain*"), in view of the Encyclopedia of Controlled Drug Delivery, vol. 1, 2 (1999) and U.S. Patent No. 5,411,981 ("*Gaillard-Kelly*"). Applicants respectfully traverse this rejection.

The Office argues that *Partain* teaches a topical film-forming controlled release composition for delivering pharmaceutical active agents and that the pharmaceutical active agents include antiacne agents, such as retinoic acid and benzoyl peroxide, and anti-alopecia agents, such as Minoxidil. Office Action at 2. According to the Office, *Partain* also teaches using solvents including ethanol and glycerin with the film-forming agent. The Office acknowledges that *Partain* does not mention that a plasticizer is used in the composition, but argues that glycerine, used in *Partain's* Example 14, is "a well-known plasticizer in [the] controlled release pharmaceutical art." *Id.* (citing the Encyclopedia of Controlled Drug Delivery, p. 307, Table 1; p. 309.)

The Office argues that *Gaillard-Kelly* teaches that the compounds of instant formula I have anti-androgenic activity, are useful in dermatology, and can be used with other antiacne components, such as retinol, or with a product stimulating the growth of hair such as Minoxidil for the treatment of alopecia.

The Office concludes that it would have been obvious to one of ordinary skill in the art to use the compounds of *Gaillard-Kelly* in the compositions of *Partain* arguing that both references "teach anti-alopecia compositions in topical formulations." Office Action at 4.

In response to Applicants arguments that the Office has failed to show that the combination of references meets all of the limitations of the instant claims, the Office argues that the Office "has produced evidence to show that 1) the use of a plasticizer in a controlled release formulation would have been obvious according to Encyclopedia of Controlled Drug Delivery; and 2) a skilled artisan in the particular art would have been aware that glycerin is a plasticizer, and 3) Partain formulation meets the instant claims as it teaches using glycerin." Applicants will address the Office's arguments below.

1. The Office has not shown that the use of a plasticizer would have been obvious in a composition according to *Partain*

The Office argues that *Partain* teaches the use of glycerin in its compositions. Because the Office believes glycerin is a plasticizer (see points 1.b and 2 below), the Office seems to conclude that *Partain* teaches compositions comprising a plasticizer.

I. The combination of references does not suggest using glycerin in a composition comprising the film-forming polymers of *Partain* and the compounds of *Gaillard-Kelly*

The Office argues that one of ordinary skill in the art would have been motivated to combine *Partain* with *Gaillard-Kelly* because “both references teach anti-alopecia compositions,” and because *Gaillard-Kelly* discloses that the instant compounds of formula I can be “combined with other hair growth agents such as Minoxidil, which is also used in *Partain*['s] invention.” Office Action at 4. The Office also argues that *Partain* “teaches a glycerin-containing controlled-release formulation, which renders the use of glycerin an obvious choice.” Office Action at 11.

It seems that the Office is using improper hindsight in making the instant rejection. “It is impermissible to use the claimed invention as an instruction manual or ‘template’ to piece together the teachings of the prior art so that the claimed invention is rendered obvious.” *In re Fritch*, 23 U.S.P.Q.2d 1780, 1784 (Fed. Cir. 1992). Instead, obviousness should be viewed through the eyes and mind of one skilled in the art back in time at the moment the invention was made, and without the benefit of the applicant's disclosure. See, e.g., *In re Dembiczak*, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). Therefore, a relevant question in this rejection is what compositions would the *Partain* and *Gaillard-Kelly* disclosures have suggested to one of ordinary skill in the art, who did not know of Applicants' invention?

As a preliminary matter, Applicants note that *Partain*'s film-forming compositions are reported to be useful for the delivery of very diverse “therapeutic actives,” such as anti-inflammatory analgesics, local anaesthetics, antibiotic agents, sulfanilamide antibacterial agents, antiviral agents, antiseptic agents, vitamin and vitamin derivatives,

anti-inflammatory corticosteroids, anti-fungal agents, vasodilators, gonadal hormones, anti-histamines, autacoids, kerolytic agents, anti-diarrhea agents, anti-alopecia agents, and moisturizing agents. *Partain* at cols. 8-9. It is important to note the vast applicability of *Partain's* compositions because the compounds of *Gaillard-Kelly* fall only among a few of the categories listed above, such as kerolytic agents (*e.g.*, anti-acne agents) and anti-alopecia agents.

Following the Office's reasoning, if one of ordinary skill in the art were to combine *Partain* with *Gaillard-Kelly* because "both references teach anti-alopecia [or acne] compositions," given the diversity of the possible different compositions available from *Partain's* disclosure, such artisan would naturally seek guidance in *Partain* regarding formulations useful for the treatment of alopecia or acne. *Partain's* Examples 7, 15, 17, and 19 fit this category. Notably, none of these formulations comprises glycerin. *Partain* only discloses the *optional* use of glycerin, among a large number of other potential components, as a diluent or as an adjuvant. *Partain* at col. 9, lines 58-68; col. 10. lines 16-22.

The only composition comprising glycerin disclosed in *Partain* is Example 14, which refers to an *antihistamine* lotion. The use of glycerin in an antihistamine lotion would not have suggested the use of glycerin in lotions useful for the treatment of alopecia or acne. In fact, there is nothing in the cited art that would have suggested the use of glycerin to one of ordinary skill in the art when preparing a composition of *Partain* comprising the *anti-androgenic* compounds disclosed in *Gaillard-Kelly*.

The Office is reminded that "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also

suggests the desirability of the combination. M.P.E.P. § 2143.01.III (internal citations omitted, emphasis added). The Office has not provided any reason supporting the desirability of having glycerin in such compositions.

Given that *Partain's* compositions do not require glycerin, and that glycerin is disclosed only for an *antihistamine* lotion, the Office's suggestion to chose glycerin as a component in a composition comprising the *anti-androgenic* compounds of *Gaillard-Kelly* seems entirely in hindsight. Effectively, the Office has selected glycerin out of several dozens of other optional excipients disclosed in *Partain*, arguing that such selection would have been an obvious choice. For a description of additives, adjuvants, diluents, etc. disclosed in *Partain* see, for example, *Partain* at col. 9, line 22 to col. 10, line 22.

The proposition that glycerin *could* have been added to *Partain's* compositions, as argued by the Office, does not mean that one skilled in the art *would* have done so in compositions comprising the *anti-androgenic* compounds of *Gaillard-Kelly*. See *Ex parte Marinaccio*, 10 U.S.Q.P.2d 1716, 1717 (Bd. Pat. App. & Int'f. 1989), stating that "the question of obviousness under 35 U.S.C. 103 is not what a routineer *could* have done but what it *would* have 'been obvious' for such a person to do." (Emphasis added.)

Indeed, "a rejection cannot be predicated on the mere identification . . . of individual components of claimed limitations, rather *particular findings must be made as to the reason* the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed." *In re Kotzab*, 55 U.S.P.Q.2d 1313, 1317 (Fed. Cir. 2000). No such reason has been identified by the

Office here, and the cited art fails to suggest the desirability of making that specific choice.

For at least the foregoing reasons, the combination of the cited references does not meet all of the limitations of the claims and Applicants respectfully request that this rejection be withdrawn.

ii. Even if the combination of references results in a composition comprising glycerin, such composition would not necessarily comprise a plasticizer

Even assuming, *arguendo*, that one of ordinary skill in the art prepared a composition according to *Partain* comprising the compounds of *Gaillard-Kelly* and glycerin, such composition would not necessarily comprise a plasticizer.

The Office argues that according to the Encyclopedia of Controlled Drug Delivery, "it is well known and respected in applicants' art [that] glycerin is a plasticizer." Office Action at 12 (emphasis in original). Applicants respectfully disagree.

The Encyclopedia of Controlled Drug Delivery does not state that glycerin "*is* a plasticizer," but that "[t]his multipurpose excipient *has been used* as a plasticizer" (p. 309). That there are certain circumstances glycerin has been so used does not imply that glycerin always acts as a plasticizer.

Specifically, the Encyclopedia of Controlled Drug Delivery clarifies that substance acting as a plasticizer in one particular formulation may not be a plasticizer in a different formulation. The Encyclopedia explains that "[p]lasticizers must be compatible, in terms of solubility parameter, with the [controlled release] polymer to which they are added to make it more flexible. Thus, plasticizers are not general purpose but must be chosen

from materials that have been shown to be useful for a particular polymer.” *Id.* at p. 307 (emphasis added). Accordingly, even if glycerin has been used as a plasticizer in some formulations, glycerin *is not always a plasticizer*.

The Office also seems to be relying on inherency to argue that the combined references meet the “at least one plasticizer” limitation in the instant claims. Neither *Partain* nor *Gaillard-Kelly* disclose or suggest the use of plasticizers in any kind of formulation. The Office seems to argue that, although none of the cited references teach the presence of a plasticizer, such limitation would be inherently present once the references have been combined.

It is generally improper to rely on inherency to establish obviousness, as explained in the next section. However, even if inherency were available in the present circumstances, the combination of references fails to meet the inherency standard.

To establish inherency, the Office needs to show, *inter alia*, that “the allegedly inherent characteristic necessarily flows from the teachings in the applied prior art.” M.P.E.P. § 2112 (emphasis in original). Because glycerin *is not always a plasticizer*, then the presence of a plasticizer does not necessarily flow from the combination of references. For at least this independent reason, the combination of references does not render obvious the instant invention and Applicants respectfully request that this rejection be withdrawn.

iii. Inherency arguments are improper in an obviousness rejection

In order for an invention to be obvious, one of ordinary skill in the art, at the relevant time period, must necessarily have been aware that the particular combination

of references would produce an item (composition, process, etc,) having all of the limitations of the claimed invention. The M.P.E.P. points out that "[o]bviousness cannot be predicated on what is not known at the time an invention was made, even if the inherency of a certain feature is later established." M.P.E.P. § 2141.02.V. The Federal Circuit and its predecessor court have long noted that "inherency is quite immaterial if . . . one of ordinary skill in the art would not appreciate or recognize that inherent result." *In re Naylor*, 152 U.S.P.Q. 106, 108 (C.C.P.A. 1966). Properties that "may be inherent [are] not necessarily known. Obviousness cannot be predicated on what is unknown." *In re Shetty*, 566 F.2d 81, 86, 195 U.S.P.Q. 753, 757, (C.C.P.A. 1977), quoting *In re Spormann*, 363 F.2d 444, 448, 150 U.S.P.Q. 449, 452 (C.C.P.A. 1966).

Therefore, the Office cannot argue that the combination of the cited references teaches all of the limitations of the instant claims because, based on section 1.b above, one of ordinary skill in the art would not have recognized that, even if glycerin was present, the composition would have necessarily comprised a plasticizer. See M.P.E.P. § 2141.02.V.

For at least this independent reason, the combination of references does not render obvious the instant invention and Applicants respectfully request that this rejection be withdrawn.

2. Response to other arguments by the Office

The Office argues that "the claimed invention is directed to a composition, and the intended use of a particular component in the prior art composition cannot be the basis for a patentable distinction." Office Action at 12. However, the recitation of "at

least one plasticizer" in the instant claims is not an "intended use of a particular component in the prior art composition," as is believed by the Office, but rather a requirement that the composition comprises at least one plasticizer. The Office is respectfully reminded that when comparing the invention with the prior art in an obviousness analysis, the invention as a whole must be considered.

M.P.E.P § 2142.02.I. Failing to take into account recited limitations falls short of considering the invention as a whole. *Id.* at § 2142.02.II.

Therefore, Applicants respectfully request that the Office give full weight to the "at least one plasticizer" limitation.

b. Claim 14

The Office rejected claim 14 under 35 U.S.C. 103(a) as allegedly being unpatentable over *Gaillard-Kelly*, *Partain*, and the Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 7, 8, 11-13, 16, 17, 22, 23, 28, and 29 above, and further in view of U.S. Patent No. 5,916,910 ("*Lai*")

The Office admits that the "combined references fail to teach angiotensin converting enzyme inhibitors." Office Action at p. 5. However, the Office argues that "*Lai* teaches conjugates of dithiocarbamates [such as captopril] with pharmacologically active agents, wherein dithiocarbamates are said to reduce cutaneous irritation and alopecia." Office Action at 4-5.

The Office further argues that it would have been obvious to one of ordinary skill in the art "to have modified the teachings of the combined references by adding to the composition captopril as motivated by *Lai* because all the references are directed to

treating alopecia, and Lai teaches captopril [is] combined with other anti-alopecia agents." *Id.* at p. 5-6.

The Office refuses to accept Applicants' arguments demonstrating that *Lai* does not disclose that dithiocarbamates reduce cutaneous irritation or alopecia. Applicants respectfully traverse this rejection.

The Office has failed to recognize that the administration of the anti-cancer agent adriamycin (chemotherapy) causes hair loss. *See, e.g.*, section D of the CCO Formulary entry for Adriamycin (2000) (previously submitted to the Office). *Lai's* invention is directed to the chemical modification of the anti-cancer agent by covalently binding a dithiocarbamate to the anti-cancer agent. *See, e.g., Lai* at col. 3, lines 61-64. According to *Lai*, the resulting anti-cancer agent conjugated to the dithiocarbamate shows a reduction in side effects, among which is a reduction in hair loss. *Id.* at col. 3, lines 48-57. Thus, *Lai* does not teach that dithiocarbamates by themselves reduce cutaneous irritation and alopecia, but rather that an anti-cancer agent conjugated to a dithiocarbamate shows lower side effects. In no event does *Lai* administer dithiocarbamates by themselves to treat alopecia.

Therefore, because *Lai* is not directed to treating alopecia, one of ordinary skill in the art would not have combined *Lai* with the teachings of *Partain* and *Gaillard-Kelly*. Moreover, even if these references were combined, the result would not be a composition comprising at least one angiotensin converting enzyme inhibitor as recited in claim 14, but a composition comprising a dithiocarbamate covalently conjugated to a compound of *Gaillard-Kelly*, which is a different chemical entity from the recited

angiotensin converting enzyme inhibitors. Therefore, such composition would fail to meet all of the limitations of claim 14.

Additionally, claim 14 depends from claim 1, which as explained in section II.a above, would not have been obvious in light of the cited references, at least because the combined references fail to teach a composition comprising a plasticizer. *Lai* was cited only for its alleged disclosure of captopril in the treatment of alopecia and fails to cure the deficiencies of the rest of the cited references. Therefore, because claim 14 incorporates the subject matter of claim 1, and claim 1 is not obvious over the cited art, claim 14 cannot be obvious in light of the cited references either.

For the foregoing reasons, the Office has not proved a *prima facie* case of obviousness in this rejection and Applicants respectfully request that the rejection be withdrawn.

c. Claim 15

The Office rejected claim 15 under 35 U.S.C. 103(a) as allegedly being unpatentable over *Gaillard-Kelly*, *Partain*, and the Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 7, 8, 11-13, 16, 17, 22, 23, 28, and 29 above, and further in view of US Patent No. 5,541,220 ("*Ismail*").

The Office admits that *Gaillard-Kelly*, *Partain*, and the Encyclopedia of Controlled Drug Delivery fail to teach methylxanthine compounds. The Office argues, however, that *Ismail* teaches agents for the treatment or protection of the skin and that *Ismail* exemplifies "a capsule that can treat alopecia comprising pentoxifylin, vitamin E, and other ingredients." Office Action at p. 6.

The Office argues that it would have been obvious to one of ordinary skill in the art to add pentoxifylin to the composition of the combined references because *Ismail* and the references are directed to treating alopecia and *Ismail* teaches pentoxifyline as increasing blood circulation. The Office further argues that the skilled artisan would have been motivated to add pentoxifyline to the composition of the combined references because of the expectation of circulating the active agents of the composition through the body. Applicants respectfully traverse this rejection.

Claim 15 depends from claim 1, which as explained in section II.a above, would not have been obvious in light of the cited references, at least because the combined references fail to teach a composition comprising a plasticizer. *Ismail* was cited only for its disclosure of pentoxifyline and fails to cure the deficiencies of the rest of the cited references. Therefore, because claim 15 incorporates the subject matter of claim 1, and claim 1 is not obvious over the cited art, claim 15 cannot be obvious in light of the cited references either.

For the foregoing reasons, the Office has not proved a *prima facie* case of obviousness in this rejection and Applicants respectfully request that the rejection be withdrawn.

d. Claims 18 and 19

The Office rejected claims 18 and 19 under 35 U.S.C. 103(a) as allegedly being unpatentable over *Gaillard-Kelly*, *Partain*, and the Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 7, 8, 11-13, 16, 17, 22, 23, 28, and 29 above, and further in view of EP 0427625 A.

The Office acknowledges that *Gaillard-Kelly*, *Partain*, and the Encyclopedia of Controlled Drug Delivery fail to teach 2,4-diamino-6-butoxy-3-sulfopyrimidine hydroxide. Office argues, however, that EP 0427625 A "teaches internal salts of 2,4-diamino-6-alkoxy-3-sulfoxypyrimidine hydroxide for combating hair loss and inducing/stimulating hair growth." Office Action at 6.

The Office further argues that it would have been obvious to one of ordinary skill in the art to add the 2,4-diamino-6-butoxy-3-sulfopyrimidine hydroxide to the composition of the combined references because EP 0427625 A and the rest of the references are all directed toward combating hair loss.

Applicants respectfully traverse this rejection. Claims 18 and 19 depend from claim 1, which as explained in section II.a above, would not have been obvious in light of the cited references at least because the combined references fail to teach a composition comprising a plasticizer. EP 0427625 A was cited only for its disclosure of 2,4-diamino-6-butoxy-3-sulfopyrimidine hydroxide and fails to cure the deficiencies of the rest of the cited references. Therefore, because claims 18 and 19 incorporate the subject matter of claim 1, and claim 1 is not obvious over the cited references, claims 18 and 19 cannot be obvious in light of the cited references either.

For the foregoing reasons, the Office has not proved a *prima facie* case of obviousness in this rejection and Applicants respectfully request that the rejection be withdrawn.

e. Claims 18 and 20

The Office rejected claims 18 and 20 under 35 U.S.C. 103(a) as allegedly being unpatentable over *Gaillard-Kelly, Partain*, and the Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 7, 8, 11-13, 16, 17, 22, 23, 28, and 29 as above, and further in view of WO 92/21317.

The Office admits that *Gaillard-Kelly, Partain*, and the Encyclopedia of Controlled Drug Delivery fail to teach 2,4-diamino-4-piperidinopyridine 1-oxide. The Office argues, however, that WO 92/21317 teaches compositions containing a pyridine 1-oxide for combating hair loss and inducing/stimulating hair growth. The Office further argues that the reference specifically discloses 2,4-diamino-4-piperidinopyridine 1-oxide.

The Office argues that it would have been obvious to one of ordinary skill in the art to add the 2,4-diamino-4-piperidinopyridine 1-oxide to the composition of the combined references because WO 92/21317 and the references are all directed toward combating hair loss.

Applicants respectfully traverse this rejection. Claims 18 and 19 depend from claim 1, which as explained in section II.a above, would not have been obvious in light of the cited references at least because the combined references fail to teach a composition comprising a plasticizer. WO 92/21317 was cited only for its disclosure of pyridine 1-oxide compounds and fails to cure the deficiencies of the rest of the cited references. Therefore, because claims 18 and 19 incorporate the subject matter of claim 1, and claim 1 is not obvious over the cited references, claims 18 and 19 cannot be obvious in light of the cited references either.

For the foregoing reasons, the Office has not proved a *prima facie* case of obviousness in this rejection and Applicants respectfully request that the rejection be withdrawn.

f. Claims 18 and 21

The Office rejected claims 18 and 21 under 35 U.S.C. 103(a) as allegedly being unpatentable over *Gaillard-Kelly, Partain*, and the Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 7, 8, 10-13, 16, 17, 22, 23, 28, and 29 as above, and further in view of WO 91/19701.

The Office admits that the combined references fail to teach 2,6-diamino-4-butoxy-1,3,5-triazine 1-oxide. The Office argues, however, that WO 91/19701 teaches compositions containing 2, 6-diamino-1,3,5-triazine derivatives for combating hair loss and inducing/stimulating hair growth and that 2,6-diamino-4-butoxy-1,3,5-triazine 1-oxide is disclosed in the examples.

The Office argues that it would have been obvious to one of ordinary skill in the art at the time the invention was made to add 2,6-diamino-4-butoxy-1,3,5-triazine 1-oxide to the composition of the combined references because all of the references are directed toward combating hair loss.

Applicants respectfully traverse this rejection. Claims 18 and 19 depend from claim 1, which as explained in section II.a above, would not have been obvious in light of the cited references at least because the combined references fail to teach a composition comprising a plasticizer. WO 91/19701 was cited only for its disclosure of 2, 6-diamino-1,3,5-triazine derivatives and fails to cure the deficiencies of the rest of the

cited references. Therefore, because claims 18 and 19 incorporate the subject matter of claim 1, and claim 1 is not obvious over the cited references, claims 18 and 19 cannot be obvious in light of the cited references either.

For the foregoing reasons, the Office has not proved a *prima facie* case of obviousness in this rejection and Applicants respectfully request that the rejection be withdrawn.

g. Claims 5 and 6

The Office rejected claims 5 and 6 under 35 U.S.C. 103(a) as allegedly being unpatentable over *Gaillard-Kelly, Partain*, and the Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 8, 10-13, 22, 23, 28, 29, 39, and 40 as above, and further in view of Cremophor RH 40 Technical Information, 1997 ("Cremophor pamphlet").

The Office admits that the combined references fail to teach polyoxyethylene hydrogenated castor oil. The Office argues, however, that the Cremophor pamphlet teaches that "POE hydrogenated castor oil is skin compatible and solubilizes hydrophobic pharmaceuticals including vitamin A (retinoic acid)." Office Action at p. 9.

The Office argues that it would have been obvious to one of ordinary skill in the art "to modify the composition of the combined references by adding to the composition POE hydrogenated castor oil as motivated by [the Cremophor pamphlet] because (a) Gaillard, Partain, and [the Cremophor pamphlet] all teach using retinoic acid; and (b) [the Cremophor pamphlet] teaches that POE hydrogenated castor oil is a well known

solubilizer in pharmaceutical/cosmetic art, which solubilizes hydrophobic pharmaceutical agents to form a clear solution." *Id.*

Applicants respectfully traverse this rejection. Claims 5 and 6 depend from claim 1, which as explained in section II.a above, would not have been obvious in light of the cited references at least because the combined references fail to teach a composition comprising a plasticizer. The Cremophor pamphlet was cited only for its disclosure of POE hydrogenated castor oil and fails to cure the deficiencies of the rest of the cited references. Therefore, because claims 5 and 6 incorporate the subject matter of claim 1, and claim 1 is not obvious over the cited references, claims 18 and 19 cannot be obvious in light of the cited references either.

For the foregoing reasons, the Office has not proved a *prima facie* case of obviousness in this rejection and Applicants respectfully request that the rejection be withdrawn.

h. Claims 1, 2, 4, 7, 10-13, 22, 23, 28, 29, 39 and 40

The Office rejected claims 1, 2, 4, 8, 10-13, 22, 23, 28, 29, 39, and 40 under 35 U.S.C. 103(a) as allegedly being unpatentable over *Gaillard-Kelly* in view of US Patent No. 5,658,559 ("*Smith*") and the Encyclopedia of Controlled Drug Delivery.

The Office relies on the Office's previous statements regarding *Gaillard-Kelly* and the Encyclopedia of Controlled Drug Delivery summarized in section II.a above.

The Office argues that *Smith* teaches a film-forming lotion composition that forms a barrier on the surface of the skin to prevent evaporative loss of moisture from the skin. The Office further argues that *Smith* teaches polyvinylpyrrolidone/eicosene copolymers,

polyvinylpyrrolidone/vinyl acetate copolymers, and polyvinylpyrrolidone/hexadecane copolymers as barrier polymers and polysaccharide polymers for time-controlled release of therapeutic agents. The Office states that *Smith's* therapeutic agents include antiacne compounds and that *Smith's* composition "comprises water and polyhydric alcohols such as propylene glycol and glycerol (plasticizer and solvent)." Office Action at 10.

The Office concludes that it would have been obvious to one of ordinary skill in the art to modify the teachings of *Gaillard-Kelly* by formulating a topical composition comprising the compound of instant formula (I) in the film-forming lotion of *Smith* "because (a) both references are directed to acne treatment compositions; and (b) *Smith* teaches that the film-forming formulation provides controlled-release of the actives while protecting the skin and prevent loss of moisture of the skin. The skilled artisan would have had a reasonable expectation of successfully producing a stable and effective film-forming lotion which is useful for treating acne or alopecia." *Id.* at 10-11.

Applicants respectfully traverse this rejection.

1. The combined references fail to teach a composition comprising a plasticizer as instantly claimed

The issue here is again whether, even if present in the composition, glycerin would meet the limitation of "at least one plasticizer" recited in the instant claims. As explained before in section II.a.1.ii above, *glycerin is not always a plasticizer*, and therefore, the Office cannot rely on a theory of inherency to argue that the combination of references meets the "at least one plasticizer" limitation.

Smith, like *Partain*, is completely silent regarding the presence of a plasticizer in its compositions. Applicants respectfully remind the Office that to establish inherency, the Office needs to show, *inter alia*, that “the allegedly inherent characteristic necessarily flows from the teachings in the applied prior art.” M.P.E.P. § 2112 (emphasis in original). Because glycerin is not always a plasticizer, then the presence of a plasticizer does not necessarily flow from the combination of references.

The uncertainty of whether glycerin would behave as a plasticizer is even greater with *Smith* because *Smith* discloses an oil/aqueous *two-phase system*. See, e.g., *Smith* at col. 1, lines 48-51. The disclosure regarding glycerin having been used as a plasticizer in the Encyclopedia of Controlled Drug Delivery refers to *single-phase systems*, and is completely silent regarding whether glycerin can even be a plasticizer in an oil/aqueous two-phase system.

For at least the foregoing reasons, the combination of references does not render obvious the instant invention and Applicants respectfully request that this rejection be withdrawn.

2. Even if glycerin is present in a composition as suggested by the Office, there is no expectation of success that a composition as claimed would be obtained

Smith teaches that “[t]he therapeutic agents should be chemically compatible with the other ingredients of the composition (col. 4, lines 47-48), and the instant specification explains that “precipitates of the substances at the application site after evaporation of the solvent” occurred with conventional aqueous/alcoholic hair lotions. Specification at p. 3, line 25 to p. 4, line 5.

Therefore, even if the references were combined, the Office has not provided any evidence that one of ordinary skill in the art would have expected that the compounds of *Gaillard-Kelly*, which are not disclosed in *Smith*, would be compatible with the ingredients and the two-phase systems of *Smith's* compositions.

For at least this independent reason, the combination of references does not render obvious the instant invention and Applicants respectfully request that this rejection be withdrawn.

III. Conclusions

In view of the foregoing remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

As mentioned above, this Reply is accompanied by a Petition for a One-Month Extension of Time and fee payment. Please grant any extensions of time required to enter this response and charge any required fees not found herewith to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: April 13, 2007

By: Elizabeth A. Doherty
Elizabeth A. Doherty
Reg. No. 50,894

Attachments: Petition for One-Month Extension of Time